

CURRICULUM VITAE

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PROFESSIONAL EXPERIENCE

12/98-present

Vice President, Research and Development, Myogen Inc, Westminster, Colorado

Responsibilities

- Corporate Officer and member of the Myogen Executive Management Team
- Lead R&D activities focused on clinical development of one Phase II and one Phase III stage therapeutics for treatment of heart failure and related disorders; use of genomic, proteomic and biological techniques for identification of novel, disease-modifying compounds for reversal and prevention of heart failure; validation of molecular targets for drug discovery; identification of novel diagnostic markers for cardiac hypertrophy and heart failure
- Project Team Leader for Enoximone P.O. Development (until 1/00)
- Project Steering Committee member for BSF 208075
- Project Team Leader for Myosin Heavy Chain Project (collaboration between Myogen and a big pharma company)

Accomplishments

- In collaboration with Myogen scientific and medical advisory boards, established the company's Research Plan; established Target Validation techniques, HT Screening for the Company; built the R&D Group; managed external collaborations resulting in the identification of new technology for the Company.
- Project Plans for two Projects established: enoximone P.O. and Myosin Heavy Chain
- Planned and completed two successful meetings with the FDA Cardiorenal Division; resulted in agreement to proceed to Phase III with a heart failure therapeutic (enoximone); achieved alignment with the Agency on endpoints for four Phase II studies, product labelling language and scope of NDA.

6/98-11/98

Vice President, Research and Development and Boulder-Site Manager, Baxter, Hemoglobin Therapeutics Division, (Post-Baxter acquisition of Somatogen), Boulder, Colorado

Responsibilities

- Member of the Hemoglobin Therapeutics Division Management Team

- Lead Research and development activities at the Boulder-Site focused on the biological support of a Phase III-stage hemoglobin product candidate, DCLHb, research and development support for a Phase II-stage hemoglobin product candidate, rHb1.1 and research and development activities related to the discovery and advancement to clinical evaluation of a Second Generation hemoglobin product candidates
- Manage the Boulder-Site administratively, including facilities, safety, MIS and communications for R&D, Operations, Clinical, HR and Finance.

Accomplishments

Defined new Boulder-Site organization in collaboration with the hemoglobin Therapeutics Division management team

- Identified several novel Second Generation hemoglobin product candidates

12/94 -6/98

Vice President, Research and Development, Somatogen, Inc., Boulder, CO

Responsibilities

Corporate Officer and member of the Executive Management Group.

- Lead Research and Development activities at Somatogen; focused on 1) commercialization of lead product, Recombinant Human Hemoglobin (rHb 1.1) for oxygen-delivering and hematopoietic therapeutic indications 2) discovery and development of Second Generation recombinant hemoglobin products 3) development of non-hemoglobin technologies.
- Manage and coordinate Departments of Molecular Biology, Protein Engineering, Hemoglobin Research/Protein Chemistry, Pharmacology/Toxicology, Molecular Computation, Analytical Development, Purification Development, Formulation Development, and Fermentation Development (total of 65-70 people).

R&D Accomplishments

- In conjunction with the other Corporate Officers, positioned Somatogen for acquisition by Baxter Healthcare and prepared and presented the key technology summaries which lured Baxter to the table and eventually lead to an acquisition of Somatogen.
- Developed bioprocess for making clinical grade (GMP) rHb1.1 with successful scale-up demonstrating achievement of commercial expression and downstream yield targets; includes construction of host vector and strain, fermentation process, recovery and downstream purification system and associated analytical characterization; some of this was accomplished in collaboration with Eli Lilly and Co., our strategic corporate partner at that time.
- Advanced the understanding of hemoglobin biological effects including efficacy (oxygen delivery to tissue and potency), and safety related biologic effects; this work completed in support of commercial development of rHb1.1 and extended to the discovery of novel hemoglobin products.
- Initiated research on a promising new indication for rHb1.1: tumor radiation therapy sensitization.
- Initiated a drug-discovery project to identify new generation recombinant hemoglobin with enhanced therapeutic attributes; over 600 variant recombinant and

chemically modified/conjugated/cross-linked molecules constructed in three years; several lead molecules are undergoing advanced biological evaluation to ascertain suitability for human clinical testing. All have significantly improved properties.

- Three/four fold increases in rHb expression levels have been achieved (relative to commercial targets for rHb1.1).
- Completed several studies investigating the level of hematopoietic activity of rHb1.1 and other recombinant hemoglobins.
- Supervised preclinical discovery and development of a novel, in-licensed platelet substitute.

4/93 -12/94

Senior Director, Drug Discovery, Searle, Skokie, IL

Responsibilities

- Supervise the Cardiovascular Discovery Research Department (approximately 50 scientists; two sites: Skokie and St. Louis) with primary emphasis on atherosclerosis, thrombosis, arrhythmia, congestive heart failure and hyperlipidemia.
- Coordinate the process by which compounds from the Discovery Department are selected for, and transferred into, the Development Pipeline.
- Member R/D Executive Committee, Research Executive Committee and Development Executive Committee.
- Skokie Discovery Site Manager for facilities, safety and space administration.
- R/D liaison to the Corporate Licensing group.

Accomplishments

- Department Charter and Long Range Research Plan established.
- Five new Ph.D. hires in 1993 with backgrounds representing new directions in cardiovascular research (atherosclerosis/thrombosis/diabetes).
- Directed the design of a process by which Searle R/D will select Discovery stage compounds for formal Development; process consists of early toxicity, formulation, pharmacokinetic and chemical development studies of candidate molecules to optimize selection and the completion of critical analysis (development plan, marketing and financial) to support informal discussions on what to develop.
- Advanced new antiplatelet and antithrombotic agents into development (7/94); two antiplatelet compounds advanced to Phase III clinical development

8/89 - 4/93

Senior Director, Scientific and Product Affairs, Licensing/Business Development, Searle, Skokie, IL

Responsibilities

- Identification and follow-up of license and business development opportunities, with particular emphasis on Japan. Technical evaluation of all product license candidates.
- Manage process for full technical, medical and marketing review of candidates.
- Coordinate design of Development and Commercialization Plans for in-license candidates.
- Presentation of licensing opportunities to Searle top-management.

- Liaison between Licensing and Searle R/D.

Accomplishments:

- Two development collaborations initiated.
- One compound in-licensed (antidiabetic).

1/86 - 8/89

Director, Department of Cardiovascular Diseases Research, Searle, Skokie, IL

Responsibilities

- Supervise product discovery, chemical and biological research in the cardiovascular field with primary emphasis on hypertension, atherosclerosis, thrombosis and arrhythmia (staff: 45).

Accomplishments

- Four compounds into development (antihypertensive, and three antiplatelet agents).
- Two compounds in clinical study: antiarrhythmic and hypolipidemic.

9/85 - 1/86

Director, Biological Research Department, Searle, Skokie, IL

Responsibilities

- Supervised product discovery, biological research in four areas: cardiovascular, CNS, gastrointestinal and autotoxin mediated diseases (staff: 80).
- Department was reorganized 1/86 following restructuring of all R/D after Monsanto takeover of Searle.

8/83 - 9/85

Section Head Pharmacology, American Critical Care (Division of Baxter Travenol Corp) (formerly Amnar-Stone Laboratories), McGaw Park, IL

Responsibilities

- Supervised drug discovery, biological research in the cardiovascular, ophthalmic and CNS areas including beta-blockers, positive inotropic agents, antiarrhythmic agents, antiglaucoma agents and antiepileptic agents (staff: 13).

Accomplishments

- Five compounds into development (two beta-blockers, one antiglaucoma, one antiarrhythmic and one antiepileptic).
- Four IND's and one NDA (with approval).

9/80 - 8/83

Group Leader, American Critical Care (Division of American Hospital Supply Corp.) McGaw Park, IL,

Responsibilities

- Supervised drug discovery, biological research in the cardiovascular area (beta-blockers, cardiotonics and alpha blockers).

11/78 - 9/80

Senior Research Investigator, Arnar-Stone Laboratories (Division of American Hospital Supply Corp.), McGaw Park, IL,

Responsibilities

- Drug discovery in field of dopamine analogues and beta adrenergic receptor antagonists.

9/76 - 11/78

Research Investigator, Arnar-Stone Laboratories, McGaw Park, IL

Responsibilities

Drug discovery in field of dopamine analogues and beta adrenergic receptor antagonists.

DRUG DEVELOPMENT EXPERIENCE

- Project Team Leader: enoximone P.O.; Phase II for treatment of ultra-advanced heart failure (myogen).
- Project Team Leader: Second Generation recombinant hemoglobin project (Somatogen).
- Designed the process used to select compounds for formal Development and Clinical Study (Searle).
- Liaison to Development Project Teams for all cardiovascular compounds accepted for development (Searle).
- Project Team Leader (American Critical Care).
- Coordinate design of Development and Commercialization Plans for in-license candidates.
- Development of an ultra-short acting beta-blocker - responsible for organizing and tracking development of a novel compound through all stages of preclinical development (raw material supplies, pharmacology, drug metabolism/pharmacokinetics, analytical assays, formulation, stability, etc.) and initial clinical trials.
- Member of three other project teams which are responsible for the development of a vasodilator, an antiarrhythmic agent and another ultra-short acting beta-blocker.

EDUCATION

1976 Ph.D., Physiology
University of Virginia
School of Medicine, Department of Physiology
Charlottesville, Virginia

Dissertation: The Microcirculatory Basis of Functional
Hyperemia in Striated Muscle (University Microfilms #76-25012)

Thesis

Advisor: Brian R. Duling, Ph.D., Professor of Physiology

1970 B.A., Biological Sciences
Cornell University
Ithaca, New York

TRAINING

- 1996 Somatogen: Performance Management System
- 1995 Somatogen: Project Management
- 1990 Searle: Introduction to Financial Analysis in Business (AMA)
- 1989 Searle: Introduction to Licensing (LES)
- 1989 Searle: Decision Making Skills: Consensus
- 1986 Searle: Interview Selection Skills
- 1986 Searle: Personnel Management System Training
- 1983 American Hospital Supply: Corporate Middle Management Course
- 1981 American Management Association: Project Management
- 1980 American Hospital Supply: Management Style and Effectiveness Training

AWARDS

American Critical Care President's Award for Scientific and Technical Excellence - 1979

Runner-up for American Critical Care President's Award for Scientific and Technical Excellence - 1978

PROFESSIONAL ACTIVITIES

Member, Editorial Board of the Journal of Cardiovascular Pharmacology - 1984 to 1994

Ad Hoc Reviewer for Microvascular Research, the American Journal of Physiology and the Journal of Pharmacology and Experimental Therapeutics, Blood

SOCIETIES

International Society for Artificial Cells, Blood Substitutes and Immobilization Biotechnology (Scientific Steering Committee)

American Society for Pharmacology and Experimental Therapeutics

American Association for Advancement of Science

International Society for Heart Research

Licensing Executives Society

American Heart Association

PATENTS

Novel therapeutic and diagnostic agents for treatment of heart failure. Applied May, 1999.

Epoxy-Steroidal Aldosterone Antagonist and Angiotensin II Antagonist Combination Therapy for Treatment of Congestive Heart Failure. WO96/40257

SEMINARS

1. Department of Physiology, University of Virginia, Fall 1976. "The microcirculatory basis of functional hyperemia in striated muscle".
2. Department of Physiology, Medical College of Wisconsin, Fall 1977. "The microcirculatory basis of functional hyperemia in hamster striated muscle".
3. Cardiovascular Discussion Group, Skokie, IL, Fall 1982. "Mechanisms of inotropic selectivity".
4. Esmolol Symposium, Spring 1985. "Basic pharmacology of esmolol".

5. Kureha Chemical Industry, Tokyo, Fall 1989. "Platelet GPIIb/IIIa: a new target for discovery of novel antiplatelet agents".
6. University of Virginia, Graduate Study Colloquium, Winter, 1994. "Job Opportunities in the Pharmaceutical Industry."
7. IBC Conference Blood Substitute, 1996. "Measurement of the Efficacy of Hemoglobin-based Oxygen Carriers
8. International Symposium on Intensive Care and Emergency Medicine, Brussels, 1997. Preclinical update on rHb1.1
9. Tokyo Blood Substitutes Conference, 1997. "Comparison of Optro with Whole Blood using 31 P-NMR Spectroscopy"

PUBLICATIONS

1. Spath, J.A., Gorczynski, R.J. and Lefer, A.M.: Possible mechanisms of the beneficial action of glucocorticoids in circulatory shock. Surg. Gyne. and Obst., 137:597-607, 1973
2. Spath, J.A., Gorczynski, R.J. and Lefer, A.M.: Pancreatic perfusion in the pathophysiology of hemorrhagic shock. Amer. J. Physiol., 226:443-451, 1974
3. Gorczynski, R. J., Spath, J.A. and Lefer, A.M.: Vascular responsiveness of the in situ perfused dog pancreas. Europ. J. Pharmacol., 27:68-77, 1974
4. Gorczynski, R.J. and Lefer, A.M.: Properties of the reticuloendothelial system of the cat. Proceed. Soc. Exper. Biol. & Med., 147:24-28, 1974
5. Gorczynski, R.J., Klitzman, B.M. and Duling, B.R.: Interrelations between contracting striated muscle and precapillary microvessels. Amer. J. Physiol., 235:H494-H504, 1978
6. Gorczynski, R.J. and Duling, B.R.: The role of oxygen in arteriolar functional vasodilation in hamster striated muscle. Amer. J. Physiol., 235:H505-H515, 1978
7. Borgman, R.J., Erhardt, P.W., Gorczynski, R.J. and Anderson, W.G.: Cyclopropylamine hydrochloride (ASL-7003): A rigid analogy of dopamine. J. Pharm. Pharmacol., 30:193-195, 1978

8. Gorczynski, R.J., Anderson, W.G., Erhardt, P.W. and Stout, D.M.: Analysis of the cardiac stimulant properties of (3,4-dihydroxyphenyl)-cyclopropylamine (ASL-7003) and 2-Amino-6,7-Dihydroxy-1,2,3,4-Tetrahydronaphthalene (A6,7DTN). J. Pharm. Exp. Therap., 210(2):252-258, 1979
9. O'Donnell, J.P., Parehk, S., Borgman, R.J. and Gorczynski, R.J.: Synthesis and pharmacology of potential beta-blockers. J. Pharm. Science, 68(10):1236-1238, 1979
10. Erhardt, P.W., Gorczynski, R.J. and Anderson, W.G.: Conformational analogues of dopamine. Synthesis and pharmacological activity of (E)- and (Z)-2-(3,4 dihydroxyphenyl) cyclopropylamine hydrochlorides. J. Med. Chem., 22 (8):907-911, 1979
11. Reynolds, R.D. and Gorczynski, R.J.: Comparison of the autonomic effects of procainamide and N-acetylprocainamide in the dog. J. Pharm. Exp. Therap., 212:579-583, 1980
12. Reynolds, R.D., Burmeister, W.E., Gorczynski, R.J., Dickerson, D.D., Mathews, M.P. and Lee, R.J.: Effects of propranolol on myocardial infarct size with and without coronary artery reperfusion in the dog. Cardiovas. Res., 15 (8):411-420, 1981
13. Gorczynski, R.J., Anderson, W.G. and Stout, D.M.: N-aralkyl substitution of 2-amino-5,6-and -6,7-dihydroxy-1,2,3,4-tetrahydronaphthalenes. 1. Cardiac and pressor/depressor activities. J. Med. Chem., 24:835-839, 1981
14. Stout, D.M. and Gorczynski, R.J.: N-aralkyl substitution of 2-amino-5,6- and -6,7-dihydroxy-1,2,3,4-tetrahydronaphthalenes. 2. Derivatives of a hypotensive-positive inotropic agent. J. Med. Chem., 25:326-328, 1982
15. Gorczynski, R.J.: Cardiovascular pharmacology of ASL-7022, a novel catecholamine. I. Inotropic, chronotropic and pressor actions. J. Pharm. Exp. Therap., 223 (1): 7-11, 1982
16. Gorczynski, R.J. and Wroble, R.W.: Cardiovascular pharmacology of ASL-7022. II. Mechanisms of inotropic selectivity. J. Pharm. Exp. Therap., 223 (1):12-19, 1982
17. Zaroslinski, J., Borgman, R.J., O'Donnell, J.P., Anderson, W.G., Erhardt, P.W., Kam, S-T, Reynolds, R.D., Lee, R. J. and Gorczynski, R.J.: Ultra-short acting beta-blockers: A proposal for the treatment of the critically ill patient. Life Sciences, 31:899-907, 1982
18. Erhardt, P.W., Woo, C.M., Gorczynski, R.J. and Anderson, W.G.: Ultra-short-acting beta-adrenergic receptor blocking agents. 1. (Aryloxy)propanolamines containing esters in the nitrogen substituent. J. Med. Chem., 25:1402-1407, 1982

19. Erhardt, P.W., Wood, C.M., Anderson, W.G. and Gorczynski, R.J.: Ultra-short-acting beta-adrenergic receptor blocking agents. 2. (Aryloxy)propanolamines containing esters on the aryl function. J. Med. Chem., 25:1408-1412, 1982
20. Klitzman, B., Damon, D.N., Gorczynski, R.J. and Duling, B.R.: Augmented tissue oxygen supply during striated muscle contraction in the hamster: Relative contributions of capillary recruitment, functional dilation and reduced tissue PO₂. Circulation Research, 51:711, 1982
21. Lee, R.J., Gorczynski, R.J. and Reynolds, R.D.: Screening methods and test models for evaluation of cardioactive drugs. Chem. Pharm. Drugs, 7:41-100, 1986
22. Gorczynski, R.J., Shaffer, J.E. and Lee, R.J.: Pharmacology of ASL-8052, a novel beta-adrenergic receptor antagonist with an ultrashort duration of action. J. Cardiovas. Pharm., 5:668-677, 1983
23. Gorczynski, R.J.: Cardiovascular pharmacology of ACC-9089 - A novel ultra-short-acting beta-adrenergic receptor antagonist. J. Cardiovas. Pharm., 6:555-564, 1984
24. Erhardt, P.W., Woo, C.M., Matier, W. L., Gorczynski, R.J. and Anderson, W.G.: Ultra-short-acting beta-adrenergic receptor blocking agents. 3. Ethylenediamine derivatives of (aryloxy)propanolamines having esters on the aryl function. J. Med. Chem., 26:1109-1112, 1983
25. Gorczynski, R. J. and Reynolds, R.D.: Cardiovascular pharmacology of ASL-7022, III. Peripheral vascular adrenergic mechanisms. J. Pharm. Exp. Therap., 232 (3):629-635, 1985
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33. Gorczynski, R.J., Quon, C.Y., Krasula, R.W. and Matier, W.L.: Esmolol: new drugs annual. Cardiovas. Drugs, 3:99.Ed. Alexander Scriabine. Raven Press: New York, 1985
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35. Sum, C.Y. and Gorczynski, R.J.: Pharmacokinetics and pharmacodynamics of esmolol, an ultra-short acting beta-blocker. J. Pharm. Exp. Therap
36. Brown, G.S., Gorczynski, R.J., Reynolds, R.D. and Shaffer, J.E.: Comparison of the parasympatholytic activity of ACC-9358 and disopyramide. Br. J. Pharm. 87:87-95, 1986
37. Reynolds, R.D., Gorczynski, R.J. and Quon, C.Y.: Pharmacology and pharmacokinetics of esmolol. J. Clin. Pharm., 26 (A): A3-A14, 1986
38. Quon, C.Y. and Gorczynski, R.J.: Pharmacodynamics and onset of action of esmolol in anesthetized dogs. J. Pharm. Exp. Therap., 237:912-8, 1986
39. Spokas, E.G., Suleymanov, O.D., Bittner, S.E., Campion J.G., Gorczynski, R.J., Lenaers, A. and Walsh, G.M.: Cardiovascular effects of chronic high-dose atriopeptin III infusion in normotensive rats. Toxicol. Appl. Pharm., 91:305-314, 1987
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45. Sillerud, L.O., Caprihan, A., Fink-Berton, N., Springer, K., Rosenthal, G.J., and Gorczynski, R.J.: Efficacy of Recombinant Human Hemoglobin (rHb1.1) Determined by ³¹P NMR During Isovolemic Exchange Transfusion. Submitted, J. Appl. Physiology
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47. William Freytag, Ph.D., Robert F. Caspari, M.D. and Richard J. Gorczynski, Ph.D.: Recent Progress in the Development of Recombinant Human Hemoglobin (rHb1.1) as an Oxygen Therapeutic, Tokyo, 1997
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ABSTRACTS

1. Gorczynski, R.J., Spath, J.A. and Lefer, A.M.: Lack of vasodilator action of synthetic glucocorticoids in circulatory shock. Circulation Suppl., 7-8:IV-107, 1973

2. Spath, J.A., Gorczynski, R.J. and Lefer, A.M.: Pathophysiologic changes associated with pancreatic hypoperfusion in hemorrhagic shock. *Circulation Suppl.*, 7-8:IV-107, 1973
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7. Gorczynski, R.J. Anderson, W.G., Erhardt, P.W. and Stout, D.M.: The cardiac stimulant activity of (3,4-dihydroxyphenyl)-cyclopropylamine (ASL-7003) and A,6,7 DTN. *Pharmacologist*, 20:253, 1978
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13. Gorczynski, R.J. Sharer, J.E. and Lee, R.J.: ASL-8052, an ultra-short acting beta-adrenergic blocking agent. *Federation Proc.* 42, 636, 1983

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16. Shaffer, J.E., Vuong, A. and Gorczynski, R.J.: Effect of hexamethonium on the inotropic selectivity of cardiotonic agents in vivo. Presented at the Annual FASEB meeting, Anaheim, CA, April, 1985
17. Hartman, J.C., Koerner, J., Lancaster, L. and Gorczynski, R.J.: In vivo calibration of a transit time ultrasound system for measuring ascending aorta volume flow (AF). Presented at the Annual ASPET meeting, Boston, MA, August, 1985
18. Shaffer, J.E., Gorczynski, R.J. and Matier, W.L.: Antiglaucoma potential of two ultra-short acting beta adrenoreceptor antagonists. Presented at the Annual ASPET meeting, Boston, MA, August, 1985
19. Nicholson, N.S., Taite, B.B., Panzer-Knodle, S.G., King, L.W., Salyers, A.K., Gorczynski, R.J. Adams, S.P. and Feigen, L.P.: Inhibition of GPIIb/IIIa (GPIIb/IIIa) by RGDS and RGD(O-Me)Y(SC-46749). Presented at the American Heart Atherosclerosis and Thrombosis Meeting, Keystone, CO, Feb., 1989
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